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Restrictions for reimbursement of interferon-free direct-acting antiviral therapies for HCV infection in Europe

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Abstract

All-oral direct-acting antiviral (DAA) HCV therapies with cure responses of >90% is a major clinical advancement. However, the high DAA list price has led many governments to restrict their reimbursement. Study aims were to review the availability of, and national criteria for, interferon-free DAA therapy reimbursement among EU/EEA countries and Switzerland. Reimbursement documentation was reviewed from November 18, 2016 to August 1, 2017. Primary outcomes were fibrosis stage, drug or alcohol use, prescriber type, and HIV co-infection restrictions. Among European countries/jurisdictions (n=35), the most commonly reimbursed DAA was ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (94%, n=33), nearly half of countries/jurisdictions (49%, n=17) required ≥F2, 83% (n=29) had no listed drug or alcohol use restrictions, 94% (n=33) required a specialist prescriber, and 97% (n=34) had no additional restrictions for HIV-HCV co-infected persons. Findings have implications for meeting WHO targets with evidence of some countries not following the 2016 EASL HCV treatment guidelines. **Funding:** The Kirby Institute is funded by the Australian Government Department of Health. The views expressed in this publication do not necessarily represent the position of the Australian Government.

Key words: hepatitis C virus, hepatitis C treatment, direct-acting antiviral, treatment restrictions, reimbursement, Europe, liver fibrosis, alcohol use, PWID, HIV-HCV co-infection

INTRODUCTION

Over 71 million (63 – 79) people are infected with chronic hepatitis C virus (HCV) infection globally with ~704,000 (652,100 – 769,600) HCV-related deaths each year.[1-3] Compared to peginterferon-based therapies, simple, tolerable, all-oral HCV direct-acting antiviral (DAA) therapies achieve viral cure in ≥90% of patients, resulting in one of the greatest clinical advances in recent decades.[4] Broad uptake of DAA therapies has the potential to substantially reduce the global HCV disease burden, in particular, HCV-related mortality and morbidity.[5-7] However, the high list price of DAA therapies in some countries has led national governments[8, 9] to restrict patient reimbursement based on liver fibrosis severity, drug and alcohol use, and prescriber type.

A 2014 study of Medicaid reimbursement criteria for sofosbuvir in the United States (US) showed some variability by state jurisdiction.[8] The majority of states (88%) had drug and/or alcohol use restrictions, most (74%) required evidence of advanced fibrosis (≥F3), over-half (66%) had prescriber limitations, and one-quarter (25%) required HIV-HCV co-infected persons to demonstrate suppressed HIV RNA levels or be recipients of antiretroviral therapy.[8] An updated reimbursement study by Ooka et al. (2017) demonstrated that, overall, restrictions had lessened over a two year period (2014 - 2016).[10] For example, 22 states required evidence of ≥F3 in 2016 as opposed to 31 states in 2014. This updated study highlights that several criteria continue to be incongruent with clinical recommendations which state that all persons willing to be treated (and who have no treatment contraindications) should be considered for HCV therapy.[11-13]

In Europe, ~3.2 million (2.1 – 3.8) persons are estimated to have chronic HCV infection.[14] The primary HCV transmission route in the majority of European countries is injection drug

use.[15-17] Although HCV incidence is decreasing overall in Europe, rates of liver-related deaths, decompensated cirrhosis, and hepatocellular carcinoma are all projected to increase 20-30% by 2030 if broad access to DAA therapy is not achieved.[14] This, in the context of 2030 HCV global targets set by the World Health Organization (WHO) which propose: a 80% reduction in HCV incidence, 90% of persons with HCV diagnosed, 80% of persons with HCV treated, and a 65% reduction in HCV-related mortality.[18] To meet WHO targets, it will be critical that countries incorporate strategies that optimise uptake of DAA therapy, including minimising DAA reimbursement restrictions.

The aims of the study were to review the availability of interferon-free DAA therapy among European Union and European Economic Area (EU/EEA) countries and Switzerland; and to review national criteria for DAA therapy reimbursement among EU/EEA countries and Switzerland.

METHODOLOGY

Data collection

This study reviewed the availability of reimbursed DAA therapy and national criteria for DAA therapy reimbursement criteria among EU/EEA countries (including England, Northern Ireland, Scotland and Wales as separate jurisdictions) and Switzerland. Reimbursement criteria were reviewed for the following DAA regimens: sofosbuvir + ribavirin, sofosbuvir/ledipasvir ± ribavirin, sofosbuvir/velpatasvir ± ribavirin, ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin, elbasvir-grazoprevir ± ribavirin, and sofosbuvir + daclatasvir ± ribavirin.

From November 18, 2016 to August 1, 2017, most data were extracted from publicly available documentation from government websites and online drug formularies with the assistance of study authors [see appendix p.1]. Supporting documentation, e.g. national HCV guidelines, was also collected when available [see appendix p.3]. If challenges arose in recovering information, one of three study authors contacted the study author from the country of interest to enable access. Given that most documentation was in a language other than English, study authors were fundamental to identifying documents of relevance. Independent document searches were conducted by three study authors to further corroborate search findings. Study authors of each country were also contacted to provide clarification if there were inconsistencies between documents and/or additional documentation was needed. In the event that documentation for a country could not be located, this finding was categorised as 'Not available'.

Information was reviewed to determine the availability of reimbursed HCV DAAs in Europe (categories were: Yes; No). In the event that an individual could retrieve access to a specific

therapy (e.g. sofosbuvir + daclatasvir ± ribavirin) but this therapy was not reimbursed, this was categorised as 'No'. Based on prior HCV DAA reimbursement studies,[8, 9] primary outcomes were criteria restrictions based on: 1) minimum fibrosis stage [METAVIR or equivalent; Meta-Analysis of Histologic Data in Viral Hepatitis]; 2) drug and/or alcohol use; 3) prescriber type; and 4) HIV co-infection. If information for a specific outcome was not reported with the remaining outcomes, this outcome was categorised as 'None listed'. Regarding primary outcomes, fibrosis stage was categorised as: No restriction; F2; F3, F4; Other; None listed; Not available. Fibrosis stage could be assessed through liver biopsy, transient elastography, biomedical markers, or a combination. It was anticipated that in many countries, patients with extrahepatic manifestations (e.g. cryoglobulinemia) would have had different criteria than asymptomatic patients (e.g. different fibrosis stage restrictions). Given that the primary interest of this study was to assess criteria experienced by the majority of patients, the minimum fibrosis stage for asymptomatic patients was recorded. Drug or alcohol use was categorised as: Prioritised; No restrictions; Additional restrictions; None listed; Not available. 'Prioritised' meant that persons with drug or alcohol use dependencies had fewer restrictions for DAA therapy access than persons without drug or alcohol use dependencies. 'No restrictions' meant that persons with drug or alcohol use dependencies could receive reimbursed DAA therapies. For instance, a person who engaged in active injection drug use (or a history of injection use) could be offered DAA therapy. 'Additional restrictions' meant that persons with drug or alcohol use dependencies needed to fulfil further criteria prior to being eligible for DAA therapy. Based on prior evidence,[8, 10] study authors anticipated that one example of a drug or alcohol use restriction that may be in existence in European countries would be a mandatory period of abstinence from substance use prior to therapy (e.g. 6 month period of abstinence from drug use). In addition to this restriction, study authors made note of any other drug or alcohol use restriction that was listed in reimbursement

criteria. Prescriber type categories were: No restriction; Specialist only; None listed; Not available. 'No restriction' meant that a healthcare practitioner other than a specialist (e.g. general practitioner) could prescribe interferon-free HCV DAA therapies. 'Specialist only' meant that there was a requirement that the prescriber worked within a specialised field. Options included, but were not limited to, hepatologist, infectious disease specialist, internal medicine specialist, and gastroenterologist. If a country permitted a general practitioner to prescribe HCV DAAs but these therapies were not reimbursed, then this was categorised as a restriction (i.e. Specialist only) because we were specifically interested in access to reimbursed therapies. Moreover, the study focus was specific to prescribing; whether a general practitioner or nurse practitioner could treat and monitor a patient who received interferon-free HCV DAA therapy was not recorded. Lastly, HIV co-infection categories were: Prioritised; Eligible; None listed; Not available. 'Prioritised' meant that persons with HIV-HCV co-infection were given treatment precedence over persons with HCV mono-infection (i.e. had fewer reimbursement restrictions). 'Eligible' meant that persons with HIV co-infection had the same restriction criteria as persons with HCV mono-infection. 'Other' was also a possible category for any of the primary outcomes, when appropriate.

Data were organized with descriptive statistics with Microsoft Excel® (version 2010, Redmond, USA). With separate Excel spreadsheets, two study authors categorised the outcome criteria of ~15 European countries/jurisdictions each. Once completed, the same two study authors independently cross-checked each other's categorisation against the documentation. Study authors were then contacted by these two study authors when further clarification was required to resolve any inconsistencies. Following this stage, information was updated as appropriate. Map imagery was created with Tableau Software (version 10.2.2, Seattle, USA).

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The funding source did not have any input into the study design, data collection, data analysis, interpretation of the data, writing of the report, or the decision to submit the manuscript for publication. The corresponding author had full access to all the data in this study and had final responsibility for the decision to submit the publication.

FINDINGS

All European countries/jurisdictions (100%, n=35) provided reimbursement for DAAs to treat HCV infection. As of August 1, 2017, the most commonly reimbursed therapy was ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (94%, n=33). Sofosbuvir + daclatasvir ± ribavirin (63%, n=22) was the least likely to be reimbursed. Most countries reimbursed sofosbuvir/ledipasvir ± ribavirin (89%, n=31) and elbasvir/grazoprevir ± ribavirin (91%, n=32), and nearly three-quarters (74%, n=26) reimbursed sofosbuvir/velpatasvir ± ribavirin. Some countries, namely Estonia, Latvia, Lithuania, Malta, and Romania, had comparatively fewer therapeutic options than other countries that reimbursed all HCV DAAs [Table 1].

Nearly half of countries/jurisdictions (49%, n=17)required evidence of, at minimum, F2 (METAVIR or equivalent). More specifically, 31% (n=11) of countries/jurisdictions required a minimum stage of F2; 17% (n=6) required ≥F3; 34% (n=12) had no fibrosis stage restrictions; 14% (n=5) had an additional requirement (e.g. point system that operates regardless of fibrosis stage). One country, Malta, had a minimum fibrosis stage of F4 [Figure 1]. There were circumstances in which fibrosis stage was dependent on genotype. For example, Norway had no fibrosis stage restrictions for genotypes 1 and 4. The clinical recommendation in Norway was also age-dependent. Persons with genotype 3, <40 years, without cirrhosis, were offered peginterferon + ribavirin for 12 weeks as the first line of therapy.[19, 20] In Austria and Switzerland, the minimum fibrosis stage was contingent on the HCV DAA therapy prescribed. For instance, sofosbuvir/ledipasvir ± ribavirin and sofosbuvir/velpatasvir ± ribavirin had a minimum fibrosis stage of F2 while elbasvir/grazoprevir ± ribavirin had no fibrosis stage restrictions.[21-24]

Although 83% (n=29) of countries/jurisdictions had no listed drug or alcohol use restrictions, 17% (n=6) required abstinence of drug and alcohol use prior to treatment (e.g. ≥6 months abstinence) [Figure 2]. This could include, but was not limited to, toxicological reports (e.g. urine drug screening) every three months to verify abstinence [see appendix p.2]. Hungary, in the case of injection drug use or alcohol use, required a psychiatric consult which supported the capability and compliance for treatment. In Romania, persons with HIV-HCV co-infection had to have a negative drug test to receive reimbursed therapy; this restriction did not seem to apply to persons with HCV monoinfection. In two countries, Liechtenstein and Switzerland, people who inject drugs (PWID) were prioritised for treatment uptake with no fibrosis stage restriction for PWID specifically. In countries in which there were no written guideline regarding substance use, study authors of each respective country emphasised that whether persons were eligible for treatment was ultimately up to physician discretion.

Almost all countries/jurisdictions in Europe (94%; n=33) required a specialist, most often a gastroenterologist, hepatologist, internal medicine specialist, or infectious disease specialist to prescribe HCV DAAs [Figure 3]. England did allow prescribing by a general practitioner although specialist input from a local multi-disciplinary committee was required. Operational Delivery Networks, established by the National Health Service, England, are committees that oversee patient care and for HCV treatment. These specific networks determine who can prescribe HCV DAAs and also, prioritise patients for therapy. In Germany, all general practitioners can prescribe reimbursed HCV DAAs. Certain countries, e.g. France, did allow general practitioners trained in HCV care to monitor patients following initiation of HCV therapy. However, France still required a specialist to prescribe the DAA therapy. Some countries provided a list of specialist prescribers or alternatively, a list of specialist centres – e.g. Austria, Czech Republic, Slovakia, and Slovenia – which patients needed to attend to

receive a specialist prescription. Thus, not all specialists were in a position to prescribe HCV DAAs.

Lastly, the majority of European countries/jurisdictions (97%, n=34) had no additional restrictions for HIV-HCV co-infected persons. Among countries that had minimum fibrosis stage restrictions for HCV monoinfected persons, 26% (n=9) of these countries had no fibrosis stage restrictions for HIV-HCV co-infected persons, and hence, HIV-HCV co-infected persons were prioritised for treatment [Figure 4]. Specifically, in Belgium, Croatia, Czech Republic, Greece, Liechtenstein, Malta, Slovakia, Slovenia, and Switzerland, HIV-HCV co-infected persons were offered HCV treatment regardless of fibrosis stage. In Romania, HIV-HCV co-infected persons needed to provide evidence of a negative drug test.

DISCUSSION

This study demonstrated some similarities concerning DAA therapy access and reimbursement restrictions in Europe. Restrictions based on specialist prescribing were almost universal with 97% (n=33) of countries requiring a specialist to prescribe DAA therapy. Disease-based restrictions were common with nearly half of countries/jurisdictions (49%, n=17) restricting DAA therapy to persons with significant liver disease (≥F2). Further, nearly one-fifth of countries (17%, n=6) required patient abstinence from drug and/or alcohol use to qualify for reimbursed therapies. These restrictions are not in agreement with the 2016 European Association for the Study of Liver (EASL) Recommendations on Treatment of Hepatitis C, which state that all patients without contraindications to therapy should be offered treatment.[12] Additionally, in order to meet WHO targets of eliminating viral hepatitis as a major public health threat by 2030, these restrictions will need to be minimised.[18]

To our knowledge, this is the first study to review HCV DAA reimbursement restrictions in Europe. This study is novel and its primary findings have major potential to influence clinical practice and policy. Similar studies on DAA restrictions have been used in legal and advocacy efforts to remove (or reduce) DAA reimbursement restrictions in Canada and US.[8-10] The follow-up US reimbursement study provided evidence of states lessening (not adding) reimbursement restrictions over a mere two year period.[8, 10] This further highlights the importance of conducting this Europe study to provide a baseline from which to compare DAA access in the upcoming years. A follow-up study on DAA access and restrictions in Europe would be beneficial. There were some limitations in the present study. Given that there was no systematic repository or standardized system for the collation of reimbursement restriction information, we relied on an extensive selection of documents as well as ongoing consultation with study authors to verify data accuracy. This study was limited to written

restrictions and prescribing practices by clinicians might differ from reimbursement criteria. For instance, among countries that have no listed drug use restriction, PWID may be much less likely to be offered DAA therapy. Further, if additional restrictions were reviewed, findings might have revealed even greater reimbursement discrepancies across countries/jurisdictions. In Belgium, for example, an elastography test *and* biomarker score were required to assess fibrosis stage (or alternatively, a liver biopsy).[25] Similarly, countries may also differ on policies concerning retreatment. The present study also did not review intra-country variability. Persons who reside in rural-based areas or do not have private health insurance plans may encounter greater obstacles to reimbursed therapies. Such topics warrant further study. Research on heterogeneity in healthcare systems in Europe, specifically, how medication coverage (with varying deductible and/or co-pay arrangements) impacts treatment access at the patient level is also needed. With respect to reimbursement restrictions, we did not specifically look at the distinction between access and choice. In some countries, the available regimens might have been limited on the basis of restrictions put in place by the payer, which may have limited the selection of DAA therapies that physicians could choose to prescribe. Lastly, timeliness of data was a limitation in this study. While efforts were made to include the most current information, online information and documentation concerning DAA availability and reimbursement restrictions were frequently changing as therapies became approved and governments negotiated new agreements with pharmaceutical companies. Government ministries were not contacted to verify information, which is a noted study limitation. Nevertheless, this study provides an accurate assessment of reimbursement restrictions in Europe as of August 1, 2017.

The considerable heterogeneity in DAA availability and reimbursement restrictions observed in Europe is consistent with previous studies evaluating regional differences in reimbursement

in Canada[9] and the US.[8, 10] Of note, 97% (n=34) of countries/jurisdictions in Europe required a specialist to prescribe DAAs compared to up to 42% of provinces/territories in Canada[9] and 67% of US states.[10] Even in European countries/jurisdictions where primary care providers can prescribe, restrictions are in place through managed care networks (e.g. England) or alternatively, physicians are concerned with medical liability claims (e.g. Germany). In Australia, all medical providers (including primary care and drug/alcohol clinicians) are authorized to prescribe DAA therapy. Less experienced prescribers, however, are required to consult a gastroenterologist/hepatologist or infectious disease specialist in relation to appropriateness of DAA treatment. Under this system, an increasing proportion of DAA prescriptions are completed by primary care and non-specialist providers.[26] Several factors are likely to influence current and future prescriber patterns including involvement of non-specialists. Countries with more concentrated geography (less rural/remote regions), well developed specialist treatment centers with extensive referral pathways, and lower proportions of highly marginalized patients, may not require significant involvement of non-specialists. On the other hand, countries that expand to include non-specialists can be encouraged by evidence which demonstrates that HCV treatment outcomes by primary care providers and specialists are comparable.[27, 28]

The WHO viral hepatitis strategy states that everyone living with viral hepatitis should have access to safe, affordable, and effective care.[18] However, nearly half of European countries (49%, n=17) have restricted DAA reimbursement to persons with advanced liver disease (≥F2), which is also inconsistent with the 2016 EASL Recommendations on Treatment of Hepatitis C.[12] Limiting DAA access to patients with more advanced liver disease (and other criteria such as genotype and age as seen in Norway) is a form of prioritisation in the context of high DAA drug pricing related to concerns regarding potential health budget impact, and

presumably, an interim strategy while awaiting development of further treatment infrastructure and declines in DAA pricing. Removal of liver disease stage restrictions is likely to occur in many countries in the near future as has happened recently in France. Successful treatment of HCV infection reduces progression of liver disease[29] and lowers all-cause mortality in people with advanced liver disease.[30] Treatment of those with the greatest risk of transmission (e.g. PWID) also helps to prevent onward HCV transmission.[31] As such, broadened access to DAA therapy will yield both individual and public health benefits.

Seventeen percent (n=6) of European countries restricted access to DAA therapy among people with recent drug and/or alcohol use. Perceptions about poor adherence from ongoing substance use and risk of reinfection due to substance relapse are reasons often put forward to withhold HCV therapy from PWID.[32, 33] A study of HCV practitioners in the DAA era (72% were gastroenterology and hepatology specialists) found that only 15% were willing to treat people who were actively injecting drugs.[32] Promising data have demonstrated excellent adherence and response to DAA HCV therapy among people with recent drug use,[34-39] people receiving opioid substitution therapy,[40-48] and persons with recent injecting drug use.[49-51] Rates of reinfection among PWID are also relatively low.[52, 53] In light of this evidence, there has been some debate as to the ethical justification for withholding therapy from people with ongoing drug/alcohol use.[54]

This study has several key implications for clinicians and policy-makers. European countries should work towards removing restrictions that prevent primary care and drug/alcohol providers from prescribing DAA therapies. The 2016 EASL Recommendations on Treatment of Hepatitis C provide the guidance to ensure appropriate HCV management by medical providers.[12] Mobilising specialists to mentor/train primary care and drug/alcohol providers,

simplifying pathways for the referral of people with advanced liver disease (e.g. APRI >1) to specialists, and providing HCV education and training for nurses, primary care providers, and drug/alcohol providers would all help to enable DAA access. The upcoming availability of pan-genotypic DAA therapies will also facilitate prescribing by primary care and drug/alcohol providers.

While there is no 'one size fits all' strategy for the widespread implementation of HCV DAAs, a massive scale-up of testing, linkage to care, and treatment, particularly among high-risk groups, will be required to reduce HCV incidence, HCV prevalence, and HCV-related morbidity and mortality.[5, 17, 55, 56] Future efforts are needed to ensure appropriate monitoring and evaluation of country-level responses to HCV infection (which could then be added to national strategies and action plans) as well as the impact of DAA treatment uptake on HCV-related morbidity and mortality.[18, 57-59] Updated epidemiological data on the morbidity and mortality of HCV-related burden[14, 60] would likely further strengthen national-level policy support for broadened HCV DAA access.

DAA reimbursement restrictions throughout Europe are undoubtedly linked to the list price of DAA regimens. As a result, current reimbursement restrictions exist in most European countries related to prioritisation. The details of DAA prices (or discounts to list prices) are often not readily available, but there are considerable between-country differences in the discounts to list prices across Europe. Broad DAA access requires negotiations to lower DAA prices (or discounts to list prices) to facilitate removal of restrictions. Greater transparency in regard to these negotiations and outcomes is important for the broader strategic development towards ''access for all". The WHO mortality and incidence elimination targets are achievable and cost-effective[61] in many countries but will require the collective efforts of

researchers, healthcare providers, policy-makers, the affected community, and the pharmaceutical industry to succeed.

Contributors

Jason Grebely, Alison D. Marshall, Jeffrey V. Lazarus, Evan B. Cunningham, and Stine Nielsen contributed to study conception and design. A study concept sheet was circulated to all authors who provided comment on the study design. All authors contributed to data acquisition. Alison D. Marshall, Evan B. Cunningham, and Stine Nielsen contacted each study author from the country of interest to facilitate document access. Document searches were also conducted independently by Alison D. Marshall, Evan B. Cunningham, and Stine Nielsen to further corroborate search findings. Alison D. Marshall and Evan B. Cunningham categorized the outcome criteria of ~15 European countries/jurisdictions each and independently cross-checked each other's categorization against the documentation. Alison D. Marshall, Jason Grebely, Gregory J. Dore, Evan B. Cunningham, and Jeffrey V. Lazarus contributed to the drafting of the manuscript. All authors revised the manuscript.

Declaration of interests

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Table 1. Availability of reimbursed interferon-free DAAs for HCV infection in Europe

	HCV DAA Therapy					
	SOF + RBV	SOF/LED ± RBV	SOF/VEL ± RBV	PrOD ± RBV	EBR-GZR ± RBV	SOF + DCV ± RBV
Austria	YES	YES	YES	YES	YES$_{\mu}$	YES
Belgium	YES	YES	YES	YES	YES	YES
Bulgaria	YES	YES	NO	YES	YES	NO
Croatia	YES	YES	YES	YES	YES	NO
Cyprus	YES	YES	YES	YES	YES	NO
Czech Republic	YES	YES	YES	YES	YES	YES
Denmark	YES	YES	YES	YES	YES	YES
England	YES	YES	YES	YES	YES	YES$^{\beta}$
Estonia	NO	NO	NO	YES¶	YES¶	NO
Finland	YES	YES	YES	NO	YES	NO
France	YES	YES	YES	YES	YES	YES
Germany	YES	YES	YES	YES	YES	YES
Greece	YES	YES	YES	YES	YES	YES
Hungary	NO	YES	NO	YES	NO	NO
Iceland	YES	YES	YES	YES	YES	YES
Ireland	NO	YES	YES	YES	YES	YES
Italy	YES	YES	YES	YES	YES	YES
Latvia	NO	NO	NO	YES$^{\beta}$	YES$^{\beta}$	NO
Liechtenstein	YES	YES	YES	YES	YES$^{\mu}$	YES
Lithuania	NO	NO	NO	YES	YES$^{\beta}$	NO
Luxembourg	YES	YES	YES	YES	YES	YES
Malta	YES	YES	NO	NO	NO	NO
Netherlands	YES	YES	YES	YES	YES	YES
N. Ireland	YES	YES	YES	YES	YES	YES
Norway	YES	YES	YES	YES	YES	YES
Poland	YES	YES	NO	YES	YES	NO
Portugal	YES	YES	YES	YES	YES	YES
Romania	NO	NO	NO	YES	NO	NO
Scotland	YES	YES	YES	YES	YES	YES†
Slovakia	YES	YES	NO	YES	YES	NO
Slovenia	YES	YES	YES	YES	YES	NO
Spain	YES	YES	YES	YES	YES	YES
Sweden	YES*	YES*	YES	YES	YES	YES*
Switzerland	YES	YES	YES	YES$_{\mu}$	YES$_{\mu}$	YES
Wales	YES	YES	YES	YES	YES	YES†

βRestricted to fibrosis stage of ≥F3
*Special consideration is required
‡Need to be GT3, treatment naïve with ≥F3
µThere are no fibrosis stage restrictions for GT1 and GT4
¶Reimbursed regardless of fibrosis stage in patients with cryoglobulinemia and post orthotopic transplantation
.

[a] Fibrosis stage restrictions based on HCV genotype

[b] Fibrosis stage is included in a point system for prioritisation of DAA therapy

[c] Fibrosis stage restrictions based on HCV genotype and IL28B polymorphism

[d] Fibrosis stage restrictions based on

Figure 1. Minimum fibrosis stage required for reimbursement of interferon-free DAAs for treatment naïve patients with HCV infection in Europe

*Please note: This figure was uploaded separately

[a] Persons with HIV-HCV co-infection had to have a negative drug test in order to receive reimbursed therapy

Figure 2. Drug and alcohol restrictions for reimbursement of interferon-free DAAs for patients with HCV infection in Europe

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Figure 3. Prescriber-type restrictions for reimbursement of interferon-free DAAs for patients with HCV infection in Europe

*Please note: This figure was uploaded separately

[a] Persons with HIV-HCV co-infection had to have a negative drug test in order to receive reimbursed therapy

Figure 4. HIV co-infection restrictions for reimbursement of interferon-free DAAs for patients with HCV infection in Europe

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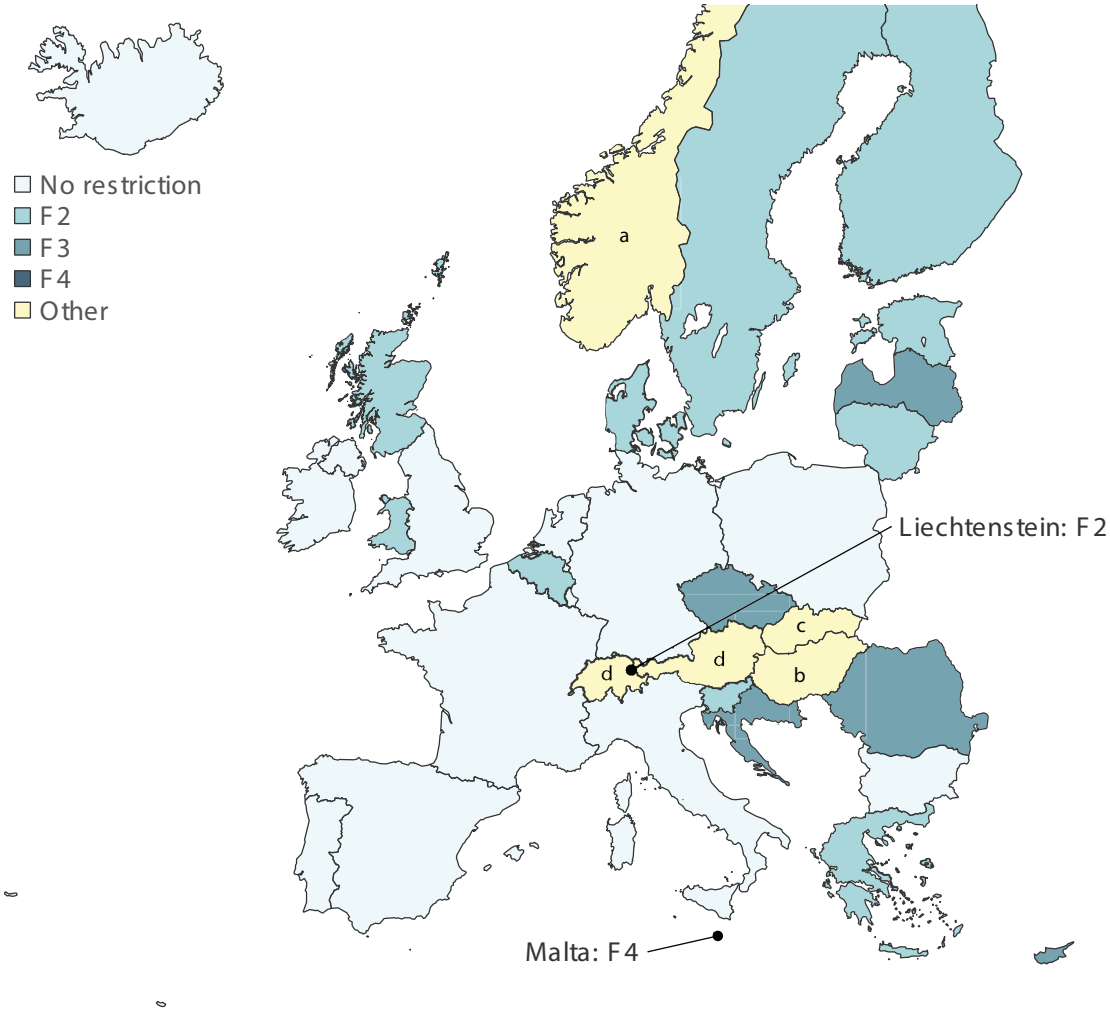
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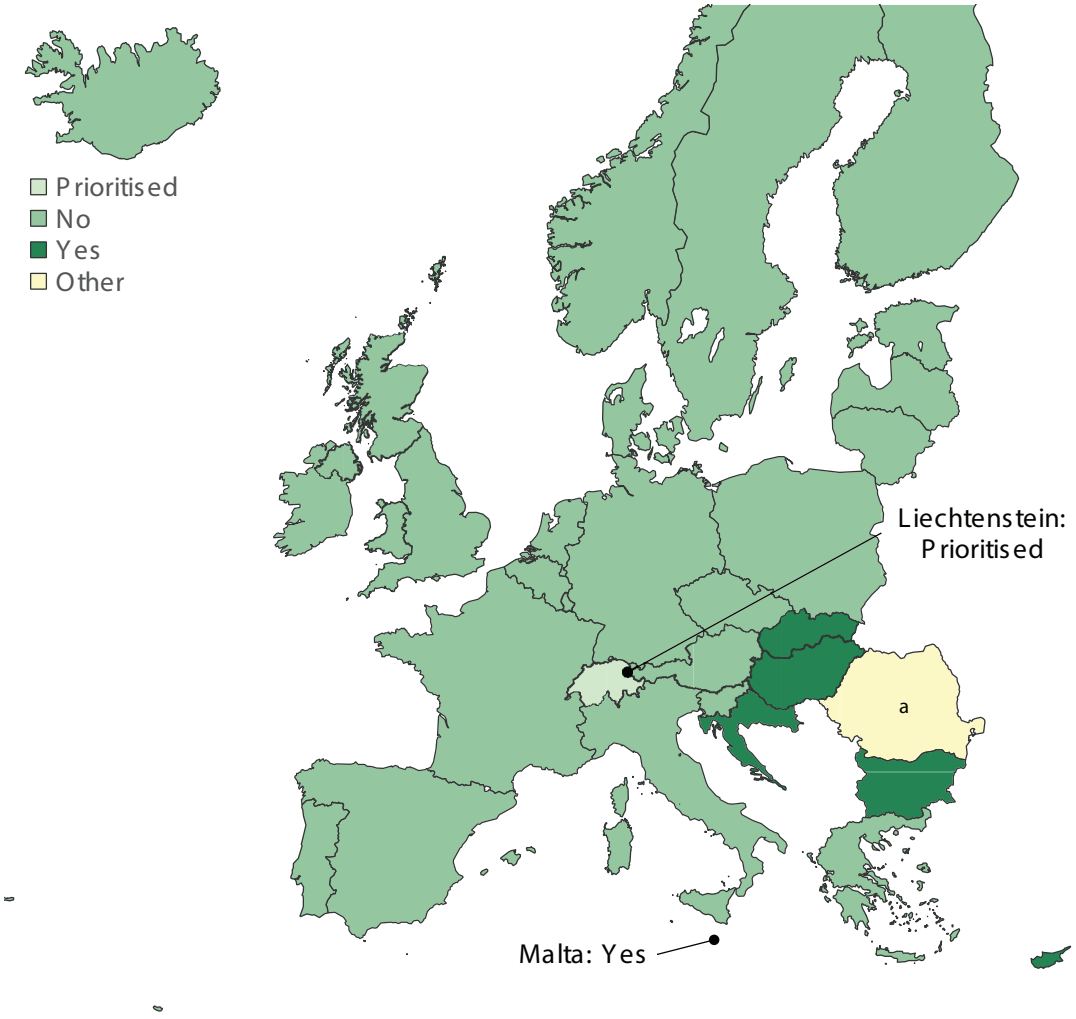
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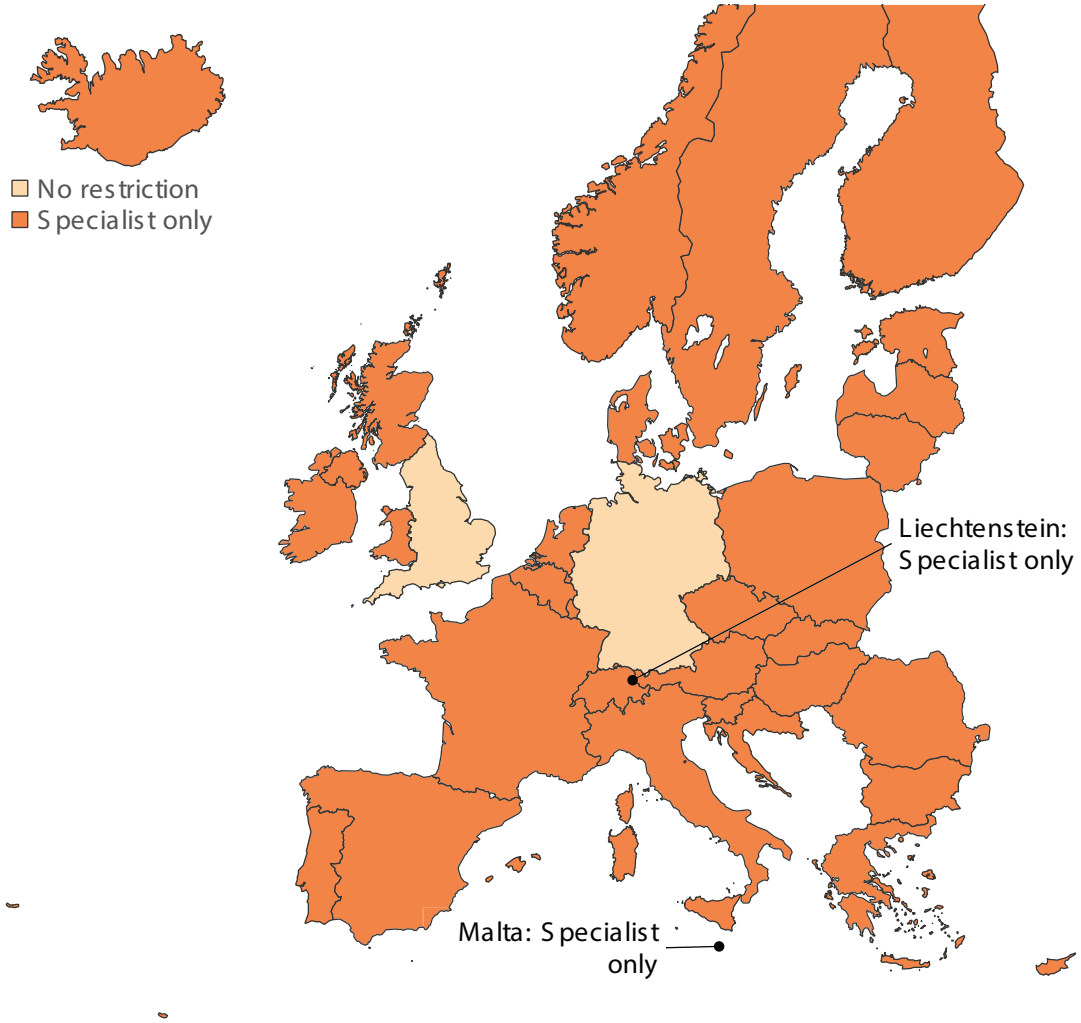
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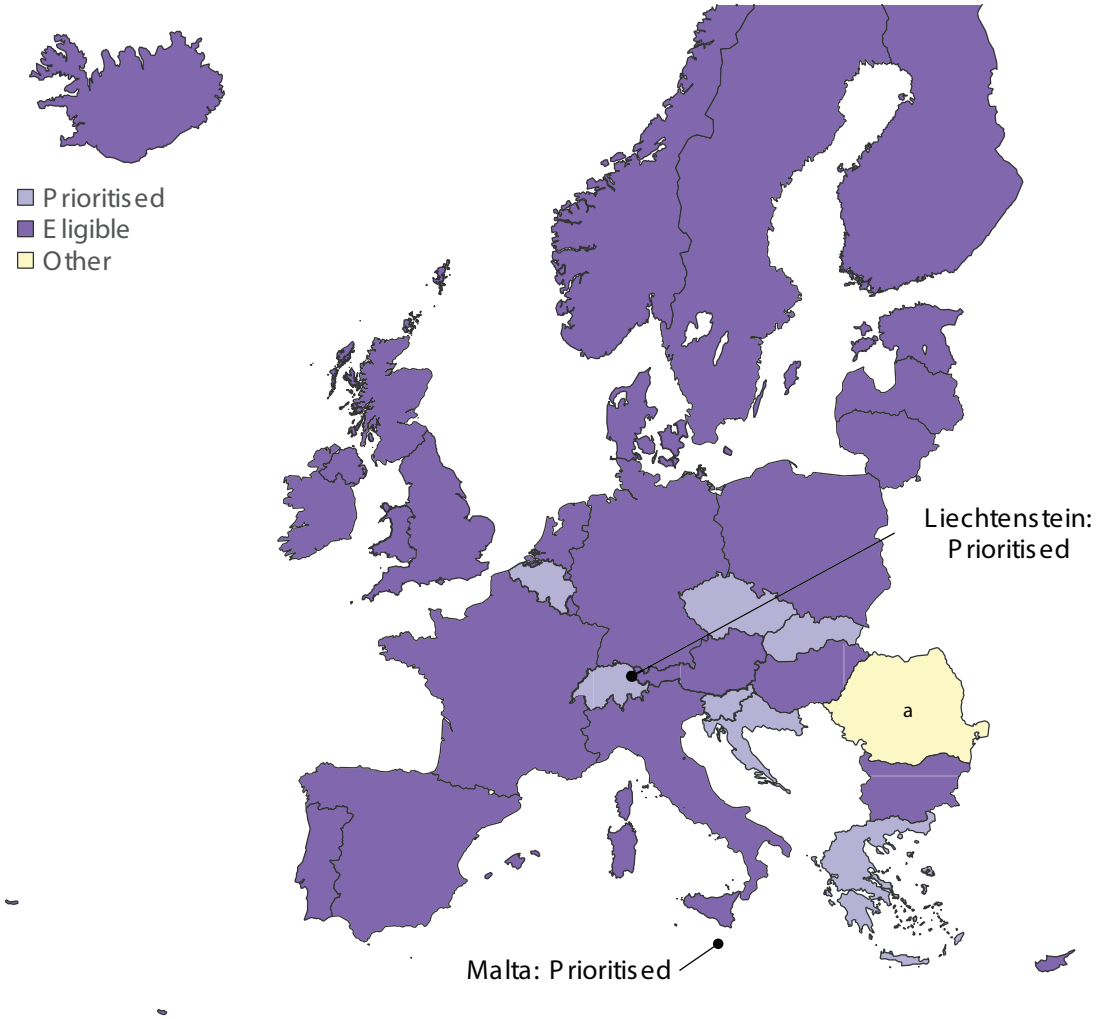
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